

<110> Beinkowski et al.

<120> ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES THEREFOR

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<150> 60/155,493

<151> 1999-09-23

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<151> 1998-09-24

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<170> PatentIn Ver. 2.0

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Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
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Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
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Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380

Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415

Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430

Gly Pro Phe Val Thr Ala Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445

Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
 450 455 460

Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
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Ile Ser Leu Leu Lys
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 <212> DNA
 <213> Homo sapiens

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<210> 10

<211> 695

<212> PRT

<213> Homo sapiens

<400> 10

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Ala Leu Glu Val Pro Thr Asp Gly Asn Ala Gly Leu Leu Ala Glu Pro
      20             25             30

Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
      35             40             45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
      50             55             60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
      65             70             75             80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
      85             90             95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
      100            105            110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
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Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
      130            135            140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
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Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
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Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
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Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
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Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
210 215 220

Val Val Glu Val Ala Glu Glu Glu Val Ala Glu Val Glu Glu Glu
225 230 235 240

Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
260 265 270

Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
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Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu
290 295 300

Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
305 310 315 320

Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg
325 330 335

Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
340 345 350

Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu
355 360 365

Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala
370 375 380

Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn
385 390 395 400

Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe
405 410 415

Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
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Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala
435 440 445

Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu
450 455 460

Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala
465 470 475 480

Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn
485 490 495

Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser
500 505 510

Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
515 520 525

Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln
530 535 540

Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn
545 550 555 560

Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr
565 570 575

Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
580 585 590

Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val
595 600 605

His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
610 615 620

Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val
625 630 635 640

Ile Val Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile
645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
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His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys
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Phe Phe Glu Gln Met Gln Asn
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      20              25              30

Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
      35              40              45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
      50              55              60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
      65              70              75              80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
      85              90              95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
      100              105              110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
      115              120              125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
      130              135              140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
      145              150              155              160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
      165              170              175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
      180              185              190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
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 Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
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 Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
 260 265 270
 Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
 275 280 285
 Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu
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 Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
 305 310 315 320
 Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg
 325 330 335
 Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
 340 345 350
 Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu
 355 360 365
 Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala
 370 375 380
 Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn
 385 390 395 400
 Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe
 405 410 415
 Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
 420 425 430
 Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala
 435 440 445
 Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu
 450 455 460
 Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala
 465 470 475 480
 Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn
 485 490 495
 Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser
 500 505 510
 Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
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Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
100 105 110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
210 215 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
225 230 235 240

Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
260 265 270

Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
275 280 285

Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu
290 295 300

Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
305 310 315 320

Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg
325 330 335

Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
340 345 350

Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu
355 360 365

Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala
370 375 380

Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn
385 390 395 400

Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe
405 410 415

Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
420 425 430

Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala
435 440 445

Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu
450 455 460

Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala
465 470 475 480

Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn
485 490 495

Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser
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Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
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Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln
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Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr
565 570 575

Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
580 585 590

Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val
595 600 605

His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
610 615 620

Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val
625 630 635 640

Ile Phe Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile
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His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
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Phe Phe Glu Gln Met Gln Asn
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<210> 16
<211> 697
<212> PRT
<213> Homo sapiens

<400> 16

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Val	Val	Glu	Val	Ala	Glu	Glu	Glu	Glu	Val	Ala	Glu	Val	Glu	Glu	Glu
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Glu	Ala	Asp	Asp	Asp	Glu	Asp	Asp	Glu	Asp	Gly	Asp	Glu	Val	Glu	Glu
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Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
580 585 590

Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val
595 600 605

His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
610 615 620

Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val
625 630 635 640

Ile Val Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile
645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
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His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys
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Phe Phe Glu Gln Met Gln Asn Lys Lys
690 695

<210> 17
<211> 2094
<212> DNA
<213> Homo sapiens

<400> 17

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 35 40 45
 Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
 50 55 60
 Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
 65 70 75 80
 Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
 85 90 95
 Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
 100 105 110
 Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
 115 120 125
 Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
 130 135 140
 Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
 145 150 155 160
 Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
 165 170 175
 Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
 180 185 190
 Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
 195 200 205
 Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
 210 215 220
 Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
 225 230 235 240
 Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
 245 250 255
 Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
 260 265 270

Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
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Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu
290 295 300

Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
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Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg
325 330 335

Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
340 345 350

Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu
355 360 365

Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala
370 375 380

Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn
385 390 395 400

Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe
405 410 415

Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
420 425 430

Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala
435 440 445

Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu
450 455 460

Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala
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Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn
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Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser
500 505 510

Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
515 520 525

Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln
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Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn
545 550 555 560

Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr
565 570 575

Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
580 585 590

Glu Val Asn Leu Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val
595 600 605

His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
610 615 620

Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val
625 630 635 640

Ile Val Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile
645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
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His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys
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Phe Phe Glu Gln Met Gln Asn Lys Lys
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<211> 2094

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<400> 20

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35 40 45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
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Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
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Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
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Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
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Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
210 215 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
225 230 235 240

Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
260 265 270

Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
275 280 285

Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu
290 295 300

Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
305 310 315 320

Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg
325 330 335

Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
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Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu
355 360 365

Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala
370 375 380

Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn
385 390 395 400

Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe
405 410 415

Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
420 425 430

Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala
435 440 445

Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu
450 455 460

Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala
465 470 475 480

Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn
485 490 495

Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser
500 505 510

Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
515 520 525

Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln
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Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn
545 550 555 560

Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr
565 570 575

Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
580 585 590

Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val
595 600 605

His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
610 615 620

Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val
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Ile Phe Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile
645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
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His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys
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Phe Phe Glu Gln Met Gln Asn Lys Lys
690 695

<210> 21

<211> 1341

<212> DNA

<213> Homo sapiens

<400> 21

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<212> PRT

<213> Homo sapiens

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His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala Pro Leu
20 25 30

Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly
35 40 45

Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser
 50 55 60
 Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr
 65 70 75 80
 Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala
 85 90 95
 Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser
 100 105 110
 Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly
 115 120 125
 Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly
 130 135 140
 Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp
 145 150 155 160
 Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala
 165 170 175
 Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp
 180 185 190
 Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu His Leu
 195 200 205
 Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val
 210 215 220
 Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly
 225 230 235 240
 Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile
 245 250 255
 Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys
 260 265 270
 Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu
 275 280 285
 Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala
 290 295 300
 Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln
 305 310 315 320
 Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val
 325 330 335
 Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile
 340 345 350
 Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr
 355 360 365
 Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly
 370 375 380

Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp
385 390 395 400

Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His
405 410 415

Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp
420 425 430

Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser
435 440 445

<210> 23

<211> 1380

<212> DNA

<213> Homo sapiens

<400> 23

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aactgggaag gcatcctggg gctggcctat gctgagattg ccaggcctga cgactccctg 600
gagcctttct ttgactctct ggtaaagcag acccacgttc ccaacctctt ctccctgcac 660
ctttgtgggt ctggcttccc cctcaaccag tctgaagtgc tggcctctgt cggaggagc 720
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<210> 24

<211> 459

<212> PRT

<213> Homo sapiens

<400> 24

Met Ala Ser Met Thr Gly Gly Gln Gln Met Gly Arg Gly Ser Met Thr
1 5 10 15

Ile Ser Asp Ser Pro Arg Glu Gln Asp Gly Ser Thr Gln His Gly Ile
20 25 30

Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg
35 40 45

Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly
50 55 60

Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met
385 390 395 400

Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg
405 410 415

Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe
420 425 430

Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp
435 440 445

Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser
450 455

<210> 25
<211> 1302
<212> DNA
<213> Homo sapiens

<400> 25
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gtggagatgg tggacaacct gaggggcaag tcggggcagg gctactacgt ggagatgacc 180
gtgggcagcc ccccgagac gctcaacatc ctggtggata caggcagcag taactttgca 240
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taccgggacc tccggaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaaggggag 360
ctgggcaccg acctggttaag catcccccat ggcccccaacg tcaactgtgcg tgccaacatt 420
gctgccatca ctgaatcaga caagttcttc atcaacggct ccaactggga aggcattctg 480
gggctggcct atgctgagat tgccaggcct gacgactccc tggagccttt ctttgactct 540
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gaggtcatca ttgtgcgggt ggagatcaat ggacaggatc tgaaaatgga ctgcaaggag 780
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<210> 26
<211> 433
<212> PRT
<213> Homo sapiens

<400> 26
Met Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly
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Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu
20 25 30
Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg
35 40 45
Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro
50 55 60
Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala
65 70 75 80

[illegible]

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<400> 28
Met Ala Ser Met Thr Gly Gly Gln Gln Met Gly Arg Gly Ser Met Thr
  1          5          10          15
Ile Ser Asp Ser Pro Leu Asp Ser Gly Ile Glu Thr Asp Gly Ser Phe
          20          25          30
Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr
          35          40          45
Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val
          50          55          60
Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe
          65          70          75          80
Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu
          85          90          95
Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu
          100          105          110
Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val
          115          120          125

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Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn
130 135 140

Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala
145 150 155 160

Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln
165 170 175

Thr His Val Pro Asn Leu Phe Ser Leu His Leu Cys Gly Ala Gly Phe
180 185 190

Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile
195 200 205

Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr
210 215 220

Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu
225 230 235 240

Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp
245 250 255

Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys
260 265 270

Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu
275 280 285

Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln
290 295 300

Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu
305 310 315 320

Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln
325 330 335

Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys
340 345 350

Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala
355 360 365

Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg
370 375 380

Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr
385 390 395 400

Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly
405 410 415

Tyr Asn Ile Pro Gln Thr Asp Glu Ser
420 425

<210> 29
<211> 1362
<212> DNA
<213> Homo sapiens

<400> 29

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ctgcggtgc cccgggagac cgacgaagag cccgaggagc ccggccggag gggcagcttt 180
gtggagatgg tggacaacct gaggggcaag tcggggcagg gctactacgt ggagatgacc 240
gtgggcagcc ccccgagac gctcaacatc ctggtggata caggcagcag taactttgca 300
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taccgggacc tccggaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaaggggag 420
ctgggcaccg acctggttaag catcccccat ggcccccaacg tcaactgtgcg tgccaacatt 480
gctgccatca ctgaatcaga caagttcttc atcaacggct ccaactggga aggcattcctg 540
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cccctcaacc agtctgaagt gctggcctct gtcggaggga gcatgatcat tggaggatc 720
gaccactgc tgtacacagg cagtctctgg tatacaccca tccggcggga gtggtattat 780
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catgtgcacg atgagttcag gacggcagcg gtggaaggcc cttttgtcac cttggacatg 1320
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<210> 30

<211> 453

<212> PRT

<213> Homo sapiens

<400> 30

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Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
          20          25          30
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
          35          40          45
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
          50          55          60
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
          65          70          75          80
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
          85          90          95
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
          100          105          110
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
          115          120          125
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
          130          135          140
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
          145          150          155          160

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Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
195 200 205

Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
210 215 220

Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
225 230 235 240

Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
245 250 255

Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
275 280 285

Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
290 295 300

Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
305 310 315 320

Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
325 330 335

Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
340 345 350

Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
355 360 365

Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
370 375 380

Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
385 390 395 400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
405 410 415

Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
420 425 430

Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
435 440 445

Gln Thr Asp Glu Ser
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<210> 31
<211> 1380
<212> DNA

<213> Homo sapiens

<400> 31

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catgtgcacg atgagttcag gacggcagcg gtggaaggcc cttttgtcac cttggacatg 1320
gaagactgtg gctacaacat tccacagaca gatgagtcac agcagcagca gcagcagtga 1380

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<210> 32

<211> 459

<212> PRT

<213> Homo sapiens

<400> 32

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Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
  1              5              10              15

Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
      20              25              30

Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
      35              40              45

Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
      50              55              60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
      65              70              75              80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
      85              90              95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
      100             105             110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
      115             120             125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
      130             135             140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
      145             150             155             160

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Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
195 200 205

Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
210 215 220

Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
225 230 235 240

Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
245 250 255

Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
275 280 285

Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
290 295 300

Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
305 310 315 320

Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
325 330 335

Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
340 345 350

Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
355 360 365

Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
370 375 380

Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
385 390 395 400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
405 410 415

Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
420 425 430

Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
435 440 445

Gln Thr Asp Glu Ser His His His His His His
450 455

<210> 33

<211> 25

<212> PRT
<213> Homo sapiens

<400> 33
Ser Glu Gln Gln Arg Arg Pro Arg Asp Pro Glu Val Val Asn Asp Glu
1 5 10 15
Ser Ser Leu Val Arg His Arg Trp Lys
20 25

<210> 34
<211> 19
<212> PRT
<213> Homo sapiens

<400> 34
Ser Glu Gln Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser
1 5 10 15
Leu Leu Lys

<210> 35
<211> 29
<212> DNA
<213> Homo sapiens

<400> 35
gtggatccac ccagcacggc atccggctg 29

<210> 36
<211> 36
<212> DNA
<213> Homo sapiens

<400> 36
gaaagctttc atgactcatc tgtctgtgga atgttg 36

<210> 37
<211> 39
<212> DNA
<213> Homo sapiens

<400> 37
gatcgatgac tatctctgac tctccgcgtg aacaggacg 39

<210> 38
<211> 39
<212> DNA
<213> Homo sapiens

<400> 38
gatccgtcct gttcacgcgg agagtcagag atagtcac 39

<210> 39
<211> 77
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Hu-Asp2

<400> 39
cggcatccgg ctgcccctgc gtagcgggtct ggggtgggtgct ccactggggtc tgcgtctgcc 60
ccgggagacc gacgaag 77

<210> 40
<211> 77
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Hu-Asp2

<400> 40
cttcgtcggg ctcccggggc agacgcagac ccagtggagc accacccaga ccgctacgca 60
ggggcagccg gatgccg 77

<210> 41
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Caspase 8
Cleavage Site

<400> 41
gatcgatgac tatctctgac tctccgctgg actctggtat cgaaaccgac g 51

<210> 42
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Caspase 8
Cleavage Site

<400> 42
gatccgtcgg ttccgatacc agagtccagc ggagagtcag agatagtcac c 51

<210> 43
<211> 32
<212> DNA
<213> Homo sapiens

<400> 43
aaggatcctt tgtggagatg gtggacaacc tg 32

<210> 44
<211> 36
<212> DNA
<213> Homo sapiens

<400> 44
gaaagctttc atgactcatc tgtctgtgga atgttg 36

<210> 45
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: 6-His tag

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ctgcggtctg	cccgggagac	cgacgaagag	cccgaaggag	ccggccggag	gggcagcttt	180
gtggagatgt	tggacaacct	gaggggcaag	tcgggggcag	gctactacgt	ggagatgacc	240
gtgggcagcc	ccccgcagac	gctcaacatc	ctgttgata	caggcagcag	taactttgca	300
gtgggtgctg	ccccccaccc	cttcctgcat	cgctactacc	agaggcagct	gtccagcaca	360

```

taccgggacc tccggaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaaggggag 420
ctggggcaccg acctggtaag catcccccat ggccccaacg tcaactgtgcg tgccaacatt 480
gctgccatca ctgaatcaga caagtctctc atcaacggct ccaactggga aggcattcctg 540
gggctggcct atgctgagat tgccaggctt tgtgggtgtg gcttccccct caaccagtct 600
gaagtgtctgg cctctgtcgg agggagcatg atcattggag gtatcgacca ctcgctgtac 660
acaggcagtc tctggtatac acccatccgg cgggagtggt attatgaggt catcattgtg 720
cgggtggaga tcaatggaca ggatctgaaa atggactgca aggagtacaa ctatgacaag 780
agcattgtgg acagtggcac caccaacctt cgtttgccca agaaagtgtt tgaagctgca 840
gtcaaatacca tcaaggcagc ctctccacg gagaagttcc ctgatggttt ctggctagga 900
gagcagctgg tgtgctggca agcaggcacc accccttggg acattttccc agtcattctca 960
ctctacctaa tgggtgaggt taccaaccag tccttccgca tcaccatcct tccgcagcaa 1020
tacctgcggc cagtggaaga tgtggccacg tcccaagacg actgttataa gtttgccatc 1080
tcacagtcac ccacgggcac tgttatggga gctgttatca tggagggctt ctacgttgtc 1140
tttgatcggg cccgaaaacg aattggcttt gctgtcagcg cttgccatgt gcacgatgag 1200
ttcaggacgg cagcgggtgga aggccctttt gtcaccttgg acatggaaga ctgtggctac 1260
aacattccac agacagatga gtcatga 1287

```

<210> 51

<211> 428

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Hu-Asp2(b)
delta TM

<400> 51

```

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
  1                      5                      10                      15
Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
                20                      25                      30
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
                35                      40                      45
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
                50                      55                      60
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
        65                      70                      75                      80
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
                85                      90                      95
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
                100                      105                      110
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
                115                      120                      125
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
                130                      135                      140
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
        145                      150                      155                      160
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
                165                      170                      175
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Leu Cys Gly
        180                      185                      190

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Ala	Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	
		195						200					205			
Ser	Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	
	210					215					220					
Trp	Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	
225					230					235					240	
Arg	Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	
				245					250					255		
Asn	Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	
			260					265					270			
Pro	Lys	Lys	Val	Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	
		275					280					285				
Ser	Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	
	290					295					300					
Cys	Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	
305					310					315					320	
Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	
				325					330					335		
Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	
			340					345					350			
Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	
		355					360					365				
Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	
	370					375					380					
Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	
385					390					395					400	
Phe	Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	
				405					410					415		
Asp	Cys	Gly	Tyr	Asn	Ile	Pro	Gln	Thr	Asp	Glu	Ser					
			420					425								

```
<210> 52
<211> 1305
<212> DNA
<213> Artificial Sequence
```

<220>
<223> Description of Artificial Sequence: Hu-Asp2(b)
delta TM

<400> 52						
atggcccaag	ccctgccctg	gctcctgctg	tggatgggcg	cgaggagtgt	gcctgccac	60
ggcaccagc	acggcatccg	gctgcccctg	cgcagcggcc	tggggggcgc	ccccctgggg	120
ctgcggctgc	cccgggagac	cgacgaagag	cccgaggagc	ccggccggag	gggcagcttt	180
gtggagatgc	tggacaacct	gaggggcaag	tcggggcagg	gctactacgt	ggagatgacc	240
gtgggcagcc	ccccgcagac	gctcaacatc	ctggtggata	caggcagcag	taacttttgc	300
gtgggtgctg	ccccccaccc	cttcctgcat	cgctactacc	agaggcagct	gtccagcaca	360
taccgggacc	tccggaagg	tgtgtatgtg	ccctacaccc	agggcaagt	ggaaggggag	420

ctgggcaccg	acctggtaa	catccccat	ggccccaacg	tactgtg	tgccaacatt	480
gctgccatca	ctgaatcaga	caagtcttc	atcaacggct	ccaactggga	aggcatcctg	540
gggtggccct	atgtctgagt	tgccaggctt	tgtggtgctg	gcttccccct	caaccagttc	600
gaagtgtctg	cctctgtcgg	agggagcatg	atcatctggag	gtatcgacca	ctcgtctgac	660
acaggcagtc	tctggtatac	accatccgg	cgggagtggt	attatgaggt	catcattgtg	720
cgggtggaga	tcaatggaca	ggatctgaaa	atggactgca	aggagtacaa	ctatgacaag	780
agcattgtgg	acagtggcac	caccaacctt	cgtttgccca	agaaagtgtt	tgaagctgca	840
gtcaaatcca	tcaaggcagc	ctctctccacg	gagaagttcc	ctgatggttt	ctggctagga	900
gagcagctgg	tgtctggcca	agcaggcacc	accccttgga	acattttccc	agtcatctca	960
ctctacctaa	tgggtgaggt	taccaaccag	tcttccgca	tcaccattct	tccgacgcaa	1020
tacctgcggc	cagtggaaga	tgtggccacg	tcccaagacg	actgttacaa	gtttgccatc	1080
tcacagtcac	ccacgggcac	tgttatggga	gctgttatca	tggagggctt	ctacgttgct	1140
tttgatcggg	cccgaataacg	aattggcttt	gctgtcagcg	cttgccatgt	gcacgatgag	1200
ttcaggacgg	cagcggtgga	aggccctttt	gtcaccttgg	acatggaaga	ctgtggctac	1260
aacattccac	agacagatga	gtcacagcag	cagcagcagc	agtga		1305

<210> 53

<211> 434

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Hu-Asp2(b)
delta TM

<400> 53

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
1. 5 10 15

Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
20 25 30

Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
35 40 45

Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
145 150 155 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Leu Cys Gly
180 185 190

Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly
 195 200 205

Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu
 210 215 220

Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val
 225 230 235 240

Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr
 245 250 255

Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu
 260 265 270

Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser
 275 280 285

Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val
 290 295 300

Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser
 305 310 315 320

Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile
 325 330 335

Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln
 340 345 350

Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val
 355 360 365

Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala
 370 375 380

Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu
 385 390 395 400

Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu
 405 410 415

Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser His His His His
 420 425 430

His His

<210> 54

<211> 2310

<212> DNA

<213> Homo sapiens

<400> 54

atgctgcccg gtttggcact gctcctgctg gccgcctgga cggctcgggc gctggaggta 60
 ccactgatg gtaatgctgg cctgctggct gaacccaga ttgccatgt ctgtggcaga 120
 ctgaacatgc acatgaatgt ccagaatggg aagtgggatt cagatccatc agggaccaa 180
 acctgcattg ataccaagga aggcacccctg cagtattgcc aagaagtcta ccctgaactg 240
 cagatcacca atgtggtaga agccaaccaa ccagtgaacca tccagaactg gtgcaagcgg 300
 ggccgcaagc agtgcaagac ccatcccccac tttgtgattc cctaccgctg cttagttggt 360

```
<210> 55
<211> 770
<212> PRT
<213> Homo sapiens
```

```

<400> 55
Met Leu Pro Gly Leu Ala Leu Leu Leu Leu Ala Ala Trp Thr Ala Arg
  1           5           10           15
Ala Leu Glu Val Pro Thr Asp Gly Asn Ala Gly Leu Leu Ala Glu Pro
      20           25           30
Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
      35           40           45
Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
      50           55           60
Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
      65           70           75           80
Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
      85           90           95
Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
      100           105           110
Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
      115           120           125

```

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
210 215 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
225 230 235 240

Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
260 265 270

Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
275 280 285

Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile
290 295 300

Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe
305 310 315 320

Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu Tyr
325 330 335

Cys Met Ala Val Cys Gly Ser Ala Met Ser Gln Ser Leu Leu Lys Thr
340 345 350

Thr Gln Glu Pro Leu Ala Arg Asp Pro Val Lys Leu Pro Thr Thr Ala
355 360 365

Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp
370 375 380

Glu Asn Glu His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala
385 390 395 400

Lys His Arg Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala
405 410 415

Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile
420 425 430

Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn
435 440 445

Glu Arg Gln Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met
450 455 460

Gln Asn
770

```
<210> 56
<211> 2253
<212> DNA
<213> Homo sapiens
```

<400> 56						
atgctgccccg	gtttggcact	gctcctgctg	gccgcctgga	cggctcgggc	gctggaggt	60
cccactgatg	gtaatgctgg	cctgctggct	gaaccccaga	ttgccatgtt	ctgtggcaga	120
ctgaacatgc	acatgaatgt	ccagaatggg	.aagtgggatt	cagatccatc	agggaccaaa	180
acctgcattg	ataccaagga	aggaactcctg	cagtatggcc	aagaagtcta	ccctgaactg	240
cagatcacca	atgtggtaga	agccaaaccaa	ccagtgacca	tccagaactg	gtgcaagcgg	300
ggccgcgaagc	agtgcaagac	ccatccccac	tttgtgattc	cctaccgctg	cttagttggt	360
gagtttgtaa	gtgatgccct	tctcgttcct	gacaagtgca	aattctttaca	ccaggagagg	420
atggatgttt	gcgaaactca	tcttcaactgg	cacaccgtcg	ccaaagagac	atgcagtgag	480
aagagtacca	acttgcatga	ctacggcatg	ttgctgcctt	gcggaattga	caagttccga	540
ggggtagagt	ttgtgtgttg	cccactggct	gaagaaagtg	acaatgtgga	ttctgctgat	600
gcggaggagg	atgactcgga	tgtctggttg	ggcggagcag	acacagacta	tgcagatggg	660
agtgaagaca	aagtagtaga	agtagcagag	gaggaagaag	tggctgaggt	ggaagaagaa	720
gaagccgatg	atgacgagga	cgatgaggat	gggtgatgagg	tagaggaaga	ggctgaggaa	780
ccctacgaag	aagccacaga	gagaaccacc	agcattgcca	ccaccaccac	caccaccaca	840
gagttctgtg	aagaggtggt	tcgagaggtg	tgtctgaac	aagccgagac	ggggccgtgc	900
cgagcaatga	tctcccgctg	gtactttgat	gtgactgaag	ggaagtgtgc	ccattctttt	960
tacggcggat	gtggcggcaa	ccggaacaac	tttgacacag	aagagtactg	catggccgtg	1020
tgtggcagcg	ccattcctac	aacagcagcc	agtacccttg	atgccgttga	caagtatctc	1080
gagacacctg	gygatgagaa	tgaacatgcc	catttccaga	aagccaaaga	gaggcttgag	1140
gccaaagcacc	gagagagaat	gtcccaggtc	atgagagaat	gggaagaggc	agaacgtcaa	1200
gcaaagaact	tgcttaaagc	tgataaagaag	cgagttatcc	agcatttcca	ggagaaagtg	1260
gaatctttgg	aacaggaagc	agccaacgag	agacagcagc	tgggtggagac	acacatggcc	1320
agagtgggaag	ccatgctcaa	tgaccgccgc	cgcttgcccc	tggagaacta	catcaccgct	1380
ctgcaggctg	ttcctcctcg	gcctcgtcac	gtgttcaata	tgctaaagaa	gtatgtccgc	1440
gcgagacaga	aggcagaca	gcacacctca	aagcatttcg	agcatgtgct	catggtggat	1500
cccaagaaaag	ccgctcagat	ccggtcccag	gttatgacac	acctccgtgt	gatttatgag	1560
cgcataatc	agtctctctc	cctgctctac	aacgtgcctg	cagtgggcga	ggagattcag	1620
gatgaagtgt	atgagctgct	tcagaaaagag	caaaactatt	cagatgacgt	cttggccaac	1680
atgattagtgt	aaccaaggat	cagttacgga	aacgatgtct	tcatgccatc	tttgaccgaa	1740
acgaaaacca	ccgtggagct	ccttcccgtg	aatggagagt	tcagccctgga	cgatctccag	1800
ccgtggtcatt	cttttggggc	tgactctgtg	ccagccaaca	cagaaaacga	agttgagcct	1860
gttgatgccc	gcctctgctg	cgaccgagga	ctgaccactc	gaccaggttc	tgggttgaca	1920
aatatcaaga	cggaggagat	ctctgaagtgt	aagatggatg	cagaattccg	acatgactca	1980
ggatatgaag	ttcatcatca	aaaattggtg	ttctttgcag	aagatgtggg	ttcaaacaaa	2040
ggtgcaatca	ttggactcat	ggtgggcggt	gttgtcatag	cgacagtgat	cgtcatcacc	2100
ctggtgatgc	tgaagaagaa	acagtaacaa	tccattcatc	atggtgtggt	ggaggttgac	2160
gccgctgtca	ccccagagga	gcgcacacctg	tccaagatgc	agcagaacgg	ctacgaaaat	2220
ccaacctaca	agttctttga	gcagatgcag	aac			2253

```
<210> 57
<211> 751
<212> PRT
<213> Homo sapiens
```

```

<400> 57
Met Leu Pro Gly Leu Ala Leu Leu Leu Leu Ala Ala Trp Thr Ala Arg
  1             5             10             15
Ala Leu Glu Val Pro Thr Asp Gly Asn Ala Gly Leu Leu Ala Glu Pro
      20             25             30
Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
      35             40             45
Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
      50             55             60

```

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
 65 70 75 80
 Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
 85 90 95
 Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
 100 105 110
 Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
 115 120 125
 Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
 130 135 140
 Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
 145 150 155 160
 Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
 165 170 175
 Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
 180 185 190
 Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
 195 200 205
 Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
 210 215 220
 Val Val Glu Val Ala Glu Glu Glu Val Ala Glu Val Glu Glu Glu
 225 230 235 240
 Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
 245 250 255
 Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
 260 265 270
 Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
 275 280 285
 Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile
 290 295 300
 Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe
 305 310 315 320
 Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu Tyr
 325 330 335
 Cys Met Ala Val Cys Gly Ser Ala Ile Pro Thr Thr Ala Ala Ser Thr
 340 345 350
 Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp Glu Asn Glu
 355 360 365
 His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys His Arg
 370 375 380
 Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala Glu Arg Gln
 385 390 395 400

Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile Gln His Phe
405 410 415

Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn Glu Arg Gln
420 425 430

Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met Leu Asn Asp
435 440 445

Arg Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu Gln Ala Val
450 455 460

Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys Tyr Val Arg
465 470 475 480

Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe Glu His Val
485 490 495

Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser Gln Val Met
500 505 510

Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser Leu Ser Leu
515 520 525

Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp Glu Val Asp
530 535 540

Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val Leu Ala Asn
545 550 555 560

Met Ile Ser Glu Pro Arg Ile Ser Tyr Gly Asn Asp Ala Leu Met Pro
565 570 575

Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro Val Asn Gly
580 585 590

Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe Gly Ala Asp
595 600 605

Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val Asp Ala Arg
610 615 620

Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu Thr
625 630 635 640

Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp Ala Glu Phe
645 650 655

Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe
660 665 670

Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val
675 680 685

Gly Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Leu Val Met Leu
690 695 700

Lys Lys Lys Gln Tyr Thr Ser Ile His His Gly Val Val Glu Val Asp
705 710 715 720

Ala Ala Val Thr Pro Glu Glu Arg His Leu Ser Lys Met Gln Gln Asn
725 730 735

Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
35 40 45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
50 55 60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
100 105 110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
210 215 220

Val Val Glu Val Ala Glu Glu Glu Val Ala Glu Val Glu Glu Glu
225 230 235 240

Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
260 265 270

Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
275 280 285

Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile
290 295 300

Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe
305 310 315 320

Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu Tyr
325 330 335

Cys Met Ala Val Cys Gly Ser Ala Met Ser Gln Ser Leu Leu Lys Thr
340 345 350

Thr Gln Glu Pro Leu Ala Arg Asp Pro Val Lys Leu Pro Thr Thr Ala
355 360 365

Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp
370 375 380

Glu Asn Glu His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala
385 390 395 400

Lys His Arg Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala
405 410 415

Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile
420 425 430

Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn
435 440 445

Glu Arg Gln Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met
450 455 460

Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu
465 470 475 480

Gln Ala Val Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys
485 490 495

Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe
500 505 510

Glu His Val Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser
515 520 525

Gln Val Met Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser
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Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp
545 550 555 560

Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val
565 570 575

Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser Tyr Gly Asn Asp Ala
580 585 590

Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro
595 600 605

Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln Pro Tyr His Ser Phe
610 615 620

Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val
625 630 635 640

Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser
645 650 655

Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp
660 665 670

Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu
675 680 685

Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly
690 695 700

Leu Met Val Gly Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Leu
705 710 715 720

Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile His His Gly Val Val
725 730 735

Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg His Leu Ser Lys Met
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Gln Asn Lys Lys
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 35 40 45
 Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
 50 55 60
 Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
 65 70 75 80
 Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
 85 90 95
 Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
 100 105 110
 Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
 115 120 125
 Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
 130 135 140
 Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
 145 150 155 160
 Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
 165 170 175
 Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
 180 185 190
 Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
 195 200 205
 Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
 210 215 220
 Val Val Glu Val Ala Glu Glu Glu Val Ala Glu Val Glu Glu Glu
 225 230 235 240
 Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
 245 250 255
 Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
 260 265 270
 Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
 275 280 285
 Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile
 290 295 300

Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe
305 310 315 320

Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu Tyr
325 330 335

Cys Met Ala Val Cys Gly Ser Ala Ile Pro Thr Thr Ala Ala Ser Thr
340 345 350

Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp Glu Asn Glu
355 360 365

His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys His Arg
370 375 380

Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala Glu Arg Gln
385 390 395 400

Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile Gln His Phe
405 410 415

Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn Glu Arg Gln
420 425 430

Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met Leu Asn Asp
435 440 445

Arg Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu Gln Ala Val
450 455 460

Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys Tyr Val Arg
465 470 475 480

Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe Glu His Val
485 490 495

Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser Gln Val Met
500 505 510

Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser Leu Ser Leu
515 520 525

Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp Glu Val Asp
530 535 540

Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val Leu Ala Asn
545 550 555 560

Met Ile Ser Glu Pro Arg Ile Ser Tyr Gly Asn Asp Ala Leu Met Pro
565 570 575

Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro Val Asn Gly
580 585 590

Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe Gly Ala Asp
595 600 605

Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val Asp Ala Arg
610 615 620

Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu Thr
625 630 635 640

Asn	Ile	Lys	Thr	Glu	Glu	Ile	Ser	Glu	Val	Lys	Met	Asp	Ala	Glu	Phe
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Arg	His	Asp	Ser	Gly	Tyr	Glu	Val	His	His	Gln	Lys	Leu	Val	Phe	Phe
			660					665					670		
Ala	Glu	Asp	Val	Gly	Ser	Asn	Lys	Gly	Ala	Ile	Ile	Gly	Leu	Met	Val
		675					680					685			
Gly	Gly	Val	Val	Ile	Ala	Thr	Val	Ile	Val	Ile	Thr	Leu	Val	Met	Leu
	690					695					700				
Lys	Lys	Lys	Gln	Tyr	Thr	Ser	Ile	His	His	Gly	Val	Val	Glu	Val	Asp
705					710					715					720
Ala	Ala	Val	Thr	Pro	Glu	Glu	Arg	His	Leu	Ser	Lys	Met	Gln	Gln	Asn
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Ser Glu Val Asn Leu Asp Ala Glu Phe Arg
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<210> 64
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Thr Gln His Gly Ile Arg
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<210> 70

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$\langle 400 \rangle$ 70

Glu Thr Asp Glu Glu Pro
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<210> 71

<211> 15

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Peptide

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Met Cys Ala Glu Val Lys Met Asp Ala Glu Phe Lys Asp Asn Pro
1 5 10 15

<210> 72

<211> 5

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: synthetic

<400> 72

Asp Ala Glu Phe Arg
1 5

<210> 73

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

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<400> 73

Ser Glu Val Asn Leu
1 5